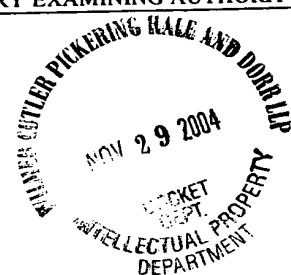


PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:
MICHAEL J. TWOMEY
HALE AND DORR LLP
60 STATE STREET
BOSTON, MA 02109



PCT

WRITTEN OPINION

(PCT Rule 66)

Applicant's or agent's file reference 110313.139WO		Date of Mailing (day/month/year) 22 NOV 2004 REPLY DUE within 1 months/days from the above date of mailing
International application No. PCT/US03/24359	International filing date (day/month/year) 04 August 2003 (04.08.2003)	Priority date (day/month/year) 07 August 2002 (07.08.2002)
International Patent Classification (IPC) or both national classification and IPC IPC(7): C07H 21/02, 21/04; C12N 15/00, 15/09, 15/63, 15/70, 15/74, 5/00, 5/02.; G01N 33/53; C12Q 1/68 and US Cl.: 536/23.1, 24/3; 435/320.1, 325, 7/1, 6; 800/13; 530/350, 387.1		
Applicant CHILDREN'S MEDICAL CENTER CORPORATION		

1. This written opinion is the first (first, etc.) drawn by this International Preliminary Examining Authority.
2. This opinion contains indications relating to the following items:
 - I ☒ Basis of the opinion
 - II ☐ Priority
 - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - IV ☐ Lack of unity of invention
 - V ☒ Reasoned statement under Rule 66.2 (a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - VI ☐ Certain documents cited
 - VII ☐ Certain defects in the international application
 - VIII ☒ Certain observations on the international application
3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. ~~The applicant may, before the expiration of that time limit, request this Authority to grant an extension. See rule 66.2(d).~~

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.
For an informal communication with the examiner, see Rule 66.6

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.
4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 07 December 2004 (07.12.2004).

Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Joanne Hama <i>Jean Proctor</i> Paralegal Specialist Telephone No. (571) 272-2911
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Form PCT/IPEA/408 (cover sheet)(July 1998)

**WILMER CUTLER PICKERING
HALE AND DORR LLP DOCKETING**

RE: 110313.139WO
 Action Date: 12-22-04
 Action to be Taken: Written Opinion
 Docketed By: BMB On: 11-29-04

WRITTEN OPINION

International application No.

PCT/US03/24359

I. Basis of the opinion

1. With regard to the elements of the international application:*

- ☒ the international application as originally filed
- ☒ the description:
 - pages 1-51, as originally filed
 - pages NONE, filed with the demand
 - pages NONE, filed with the letter of _____
- ☒ the claims:
 - pages 52-67, as originally filed
 - pages NONE, as amended (together with any statement) under Article 19
 - pages NONE, filed with the demand
 - pages NONE, filed with the letter of _____
- ☒ the drawings:
 - pages 1 and 2, as originally filed
 - pages NONE, filed with the demand
 - pages NONE, filed with the letter of _____
- ☒ the sequence listing part of the description:
 - pages 1-4, as originally filed
 - pages NONE, filed with the demand
 - pages NONE, filed with the letter of _____

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item. These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the written opinion was drawn on the basis of the sequence listing:

- ☒ contained in the international application in printed form.
- ☒ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages NONE
- ☐ the claims, Nos. NONE
- ☐ the drawings, sheets/fig NONE

5. ☐ This opinion has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed."

WRITTEN OPINION

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III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The question whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 21-25 and 101-111

because:

☐ the said international application, or the said claim Nos. _____ relate to the following subject matter which does not require international preliminary examination (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____ are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. _____.

2. A written opinion cannot be drawn due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

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V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims <u>NONE</u>	YES
	Claims <u>1-20 and 26-100</u>	NO
Inventive Step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1-20 and 26-100</u>	NO
Industrial Applicability (IA)	Claims <u>1-20 and 26-100</u>	YES
	Claims <u>NONE</u>	NO

2. CITATIONS AND EXPLANATIONS

Claims 1-20 and 26-100 lack novelty under PCT Article 33(2) as being anticipated by Ren, et al., 2001. The specification describes techniques and uses for Catsper4. However, those uses have been anticipated in the art. Ren et al. disclose the sequence for an isolated Catsper. While the specification demonstrates that there is low sequence identity between Catspers 1-4, it might be assumed, however, that the Catspers are linked as family members because they share similar domains and arrangement of these domains. For this reason, the sequence and the domains disclosed by Ren et al. anticipate the sequence and domains disclosed in the specification (claims 1-11). Ren et al. describe experiments that characterize Catsper and anticipate the Applicant's claims. Ren describes that Catsper is necessary for calcium channel influx (claims 44-45). It is well known in the art that there are standard experiments one skilled in the art would carry out to characterize a new protein. They include carrying out in situ (claims 12-14) and antibody stains to localize the nucleic acids and protein (claims 35-40); an expression vector can be used, for example, to express the nucleic acid in sites where the protein is not normally localized, or to express nucleic acids encoding domains of protein (claims 15-20), or to express proteins to which antibodies can be made (claims 29-34); to make a cell or transgenic animal that ectopically express Catsper4 or an animal that has a disruption in the Catsper4 gene (claims 26-28, 46-47).... For its role in the sperm, Catsper has been predicted by Ren et al to be a potential target for male infertility screening and treatment (claims 41-43, 48-49, 50-100).

Claims 1-20 and 26-100 meet the criteria set out in PCT Article 33(4), and thus meet industrial applicability because the subject matter claimed can be made or used in industry. The claims are to methods of treating infertility and to designing contraceptive methods.

----- NEW CITATIONS -----

WRITTEN OPINION

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VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Claims 26-28 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because claim 26 is not fully supported by the description. The description does not disclose the claimed invention in a manner sufficiently clear and complete for the claimed invention to be carried out by a person skilled in the art because: transgenic animals, other than mice, cannot be made by homologous recombination. Homologous recombination occurs in ES cells, of which, only mice is the only species in which ES cells have been cultured.

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Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

TIME LIMIT:

The time limit set for response to a Written Opinion may not be extended. 37 CFR 1.484(d). Any response received after the expiration of the time limit set in the Written Opinion will not be considered in preparing the International Preliminary Examination Report.